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FILE 'JPOABS' ENTERED AT 09:43:36 ON 16 MAY 1997
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  *     J A P A N E S E   P A T E N T   A B S T R A C T S       *
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            32 COMBINATORIAL
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           258 GENES
          3832 GENE
                 (GENE OR GENES)
          2612 LIBRARY
           105 LIBRARIES
          2634 LIBRARY
                 (LIBRARY OR LIBRARIES)
L7           0 COMBINATORIAL AND (GENE OR LIBRARY)
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          6165 GENE
                 (GENE OR GENES)
          1054 LIBRARY
           252 LIBRARIES
          1220 LIBRARY
                 (LIBRARY OR LIBRARIES)
L8          27 COMBINATORIAL AND (GENE OR LIBRARY)
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US 05523389A Jun. 4, 1996 L8: 1 of 27

Inhibitors of human immunodeficiency virus

INVENTOR: DAVID J ECKER, et al. (2)
ASSIGNEE: ISIS PHARMACEUTICALS INC
APPL NO: US 12801193A
DATE FILED: Sep. 28, 1993
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C12N 15/11; C12Q 1/68

ABSTRACT:

<CHG DATE=19960628 STATUS=N>The phosphorothioate oligonucleotide T2G4T2 was identified as an inhibitor of HIV infection in vitro by **combinatorial** screening of a **library** of phosphorothioate oligonucleotides that contained all possible 8-nucleotide sequences. The oligonucleotide forms a parallel-stranded tetrameric guanosinequartet (G-quartet) structure. Tetramer formation and the phosphorothioate backbone are essential for antiviral activity. The G-quartet structure binds to the HIV envelope protein gp120 at the V3 loop and inhibits both

cell-to-cell and virus-to-cell infection.

US 05506337A Apr. 9, 1996 L8: 2 of 27
Morpholino-subunit **combinatorial** **library** and method

INVENTOR: JAMES E SUMMERTON, et al. (1)
ASSIGNEE: ANTIVIRALS INC
APPL NO: US 24215994A
DATE FILED: May 11, 1994
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07D 413/12; C07D 413/14; C08G 59/00; C08G 65/00

ABSTRACT:

A method of generating a compound capable of interacting specifically with a selected macromolecular ligand is disclosed. The method involves contacting the ligand with a **combinatorial** **library** of oligomers composed of morpholino subunits with a variety of nucleobase and non-nucleobase side chains. Oligomer molecules that bind specifically to the receptor are isolated and their sequence of base moieties is determined. Also disclosed is a **combinatorial** **library** of oligomers useful in the method and novel morpholino-subunit polymer compositions.

US 05449754A Sep. 12, 1995 L8: 3 of 27
Generation of **combinatorial** **libraries**

INVENTOR: GARY M NISHIOKA
ASSIGNEE: H & N INSTR INC
APPL NO: US 23149494A
DATE FILED: Apr. 22, 1994
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07K 1/00

ABSTRACT:

Ink-jet printing technology is applied to the creation of multi unit chemical compound **libraries**. Ink-jet type nozzles are used to inject multiple droplets onto the surface an appropriate support, such droplets

consisting of solutions containing units of the chemical compound that will attach to the support surface. Droplets are then injected, by such nozzles, onto the support attached unit droplets that contain units that will attach to such support attached units. The second step is repeated to create multiple varying unit chemical compounds. Ink-jet printing technology allows the deposition of small droplets that do not overlap or splatter. The system is particularly useful in the creation of **libraries** of multiple peptide compounds where the units are amino acids.

US 05416719A May 16, 1995 L8: 4 of 27

Computerized generation of truth tables for sequential and **combinatorial** cells

INVENTOR: OLIVIER PRIBETICH
ASSIGNEE: VLSI TECHNOLOGY INC
APPL NO: US 99191592A
DATE FILED: Dec. 17, 1992
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL:

ABSTRACT:

A computerized method of generating a truth table of a cell in a **library** of circuit cells includes representing basic elements of the cells in a hardware description language, representing each cell as a set of equations in that language and parsing the equations each in accordance with a respective abstract data tree of which the 'leaves' or extremities are signal values or constants. The parsing of each equation yields a respective partial truth table. The partial truth tables are merged to provide a complete truth table, which is preferably subjected to Boolean and/or expression optimization to reduce the number of entries in the truth table.

US 05084824A Jan. 28, 1992 L8: 5 of 27

Simulation model generation from a physical data base of a **combinatorial** circuit

INVENTOR: NIM C LAM, et al. (1)
ASSIGNEE: NAT SEMICONDUCTOR CORP
APPL NO: US 50258190A
DATE FILED: Mar. 29, 1990
PATENT ABSTRACTS OF EUROPE

ABS [redacted]
ABS V[redacted]NO:
ABS PUB DATE:
INT-CL: G06F 15/60

ABSTRACT:

A design layout sequence for an application specific integrated circuit such as an ECL gate array includes a schematic capture step, which results in a logic netlist file, and a placement and routing step which results in a number of various files defining, for example bias drivers, I/O macros, and relationships between chip pads and I/O signals. The design layout sequence culminates in a physical data base file. To ensure a functional design, the designer's work is simulated after both schematic capture and placement and routing using a **library** containing simulation models for each type of macrocell used in the design. The gate-level netlist component of the simulation models are created automatically in a computer-implemented technique that identifies each root in the **combinatorial** circuit, assigns each a logical value, and traverses the tree that originates from each identified root. As each tree is traversed, Boolean equations identifying the logical values at each node encountered are determined in accordance with a set of relationships pertinent to the standard circuit elements and a set of logic value assignment definitions. The resulting set of Boolean equations is used to construct the gate-level netlist that is incorporated into the simulation model of the macrocell.

WO 09603424A1 Feb. 8, 1996 L8: 6 of 27

COMBINATORIAL **LIBRARIES** OF MOLECULES AND METHODS FOR PRODUCING SAME

INVENTOR: DALE L BOGER
ASSIGNEE: SCRIPPS RESEARCH INST, et al. (1)
APPL NO: US 09509541W
DATE FILED: Jul. 26, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07K 1/04; C12Q 1/68; C07D 209/04; C07D 241/12; C07D 207/32

ABSTRACT:

This invention features methods of synthesizing **combinatorial** **libraries** of chemical compounds, and **combinatorial** **libraries**

of chemical compounds formed by the methods of this invention. Specifically, Diels-Alder chemistry is utilized to generate **libraries** of diverse molecules which are easily differentially functionalized with various chemical moities and in one aspect are configured to act as non-hydrolyzable peptidomimetics.

WO 09603418A1 Feb. 8, 1996 L8: 7 of 27

SOLUBLE **COMBINATORIAL** **LIBRARIES**

INVENTOR: KIM JANDA, et al. (1)
ASSIGNEE: SCRIPPS RESEARCH INST, et al. (2)
APPL NO: US 09509614W
DATE FILED: Jul. 26, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07H 21/00; C07K 1/04

ABSTRACT:

The present invention relates to novel soluble **combinatorial** **libraries**, comprising a soluble phase in solution attached to a core molecule, and allowing the improved high-yield and efficient production of soluble **combinatorial** **libraries**. Some specific examples of the soluble **combinatorial** **libraries** claimed herein comprise one or more of the following: amino acids, alpha -azetide amino acids, triazine dione molecules, gamma -lactamtide molecules, delta -lactamthiotide molecules, beta -lactam nucleus containing molecules, lycoramine alkaloid nucleus containing molecules, and beta -blocker nucleus molecules. Further, a split synthesis technique for generating librairies of **combinatorial** molecules employs a biphasic macromolecular support which is soluble during the pooling, splitting, and coupling steps but which is insoluble during the washing step. The use of a biphasic macromolecular support in its soluble phase significantly enhances the efficiency and performance of the pooling, splitting, and coupling steps. The use of a biphasic macromolecular support in its insoluble phase significantly enhances the efficiency and performance of the washing step.

WO 09603212A1 Feb. 8, 1996 L8: 8 of 27

MULTIDIMENSIONAL CONDUIT **COMBINATORIAL** **LIBRARY** SYNTHESIS DEVICE

INVENTOR: SYDNEY BRENNER
ASSIGNEE: BRENNER SYDNEY
APPL NO: IB 09500626W

DATE FILED: Jul. 25, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: B01L 3/00; B01J 19/00; C07K 1/04

ABSTRACT:

This invention features methods and devices for rapidly, efficiently and conveniently synthesizing **combinatorial** **libraries** of chemical compounds. The present invention provides an efficient method for synthesizing N<2> or N<3> compounds. Specifically, a two-dimensional or three-dimensional conduit synthesis device is provided.

WO 09600148A1 Jan. 4, 1996 L8: 9 of 27

METHODS FOR THE SOLID PHASE SYNTHESIS OF THIAZOLIDINONES, METATHIAZANONES, AND DERIVATIVES THEREOF

INVENTOR: CHRISTOPHER P HOLMES
ASSIGNEE: AFFYMAX TECH NV, et al. (1)
APPL NO: US 09507988W
DATE FILED: Jun. 23, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: B32B 9/04

ABSTRACT:

This invention provides an efficient and versatile method for the **combinatorial** synthesis and screening of 4-thiazolidinones, metathiazanones, and derivatives thereof. In order to expediently synthesize a **combinatorial** **library** of derivatives based upon these core structures, a general methodology for the solid phase synthesis of these derivatives is also provided. Arrays of thiazolidinones, metathiazanones, and derivatives thereof useful as peptidomimetics and for the identification of agents having antifungal, antihistaminic, or antimicrobial activity or use in the treatment of inflammation, hypertension, renal failure, congestive heart failure, uremia and other conditions can be prepared using this method.

WO 09535503A1 Dec. 28, 1995 L8: 10 of 27

SYNTHESIS OF **COMBINATORIAL** **LIBRARIES**

INVENTOR: JOHN J BALDWIN, et al. (1)
ASSIGNEE: PHARMACOPEIA INC, et al. (2)
APPL NO: US 09508882W
DATE FILED: Jun. 21, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: G01N 33/53; G01N 33/531; C07K 17/00; C07H 1/00

ABSTRACT:

<CHG DATE=19960214 STATUS=O>Directly dividing the contents of each sub-pool into the sub-pools for the next step in the synthetic scheme for producing a **combinatorial** **library** reduces the standard deviation, sigma , relative to the standard deviation of the split synthesis method for producing such **libraries**.

WO 09534575A1 Dec. 21, 1995 L8: 11 of 27
COMBINATORIAL PEPTIDE **LIBRARY** AND METHOD

INVENTOR: ROBERT S HODGES, et al. (5)
ASSIGNEE: SYNTHETIC PEPTIDES INC
APPL NO: IB 09500560W
DATE FILED: Jun. 13, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07K 1/04; G01N 33/53

ABSTRACT:

A **combinatorial** **library** composition and method for using the **library** to construct oligomers effective to bind to a selected ligand is disclosed. The **library** composition includes at least two sets of **combinatorial** oligomer **libraries**, each **library** set having selected oligomer subunit positions filled by known subunits, and other subunit positions containing permutations of subunits. In the selection method, oligomers from each **library** set are identified, and a new permutation **library** formed of subunits corresponding to the highest binding affinity oligomers in each **library** is screened for binding affinity to the selected ligand.

WO 09532425A1 Nov. 30, 1995 L8: 12 of 27

ENCODED **COMBINATORIAL** **LIBRARIES**

INVENTOR: DENNIS SHINJI YAMASHITA, et al. (1)
ASSIGNEE: SMITHKLINE BEECHAM CORP, et al. (2)
APPL NO: US 09506392W
DATE FILED: May 23, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: G01N 33/53; G01N 33/545; C07K 17/08

ABSTRACT:

Invented is a method of preparing **combinatorial** **libraries** and **combinatorial** **libraries** prepared thereby. Also invented is a method for identifying compounds having desired characteristics from a **combinatorial** **library** or a set of **combinatorial** **libraries** by the use of flow cytometry. Also invented is a method for encoding **combinatorial** **libraries** using fluorophore labeled beads.

WO 09532184A1 Nov. 30, 1995 L8: 13 of 27

SYSTEMATIC MODULAR PRODUCTION OF AMINIMIDE- AND OXAZOLONE- BASED MOLECULES HAVING AT LEAST TWO STRUCTURAL DIVERSITY ELEMENTS

INVENTOR: JOSEPH C JR HOGAN
ASSIGNEE: ARQULE INC
APPL NO: US 09506208W
DATE FILED: May 18, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07C 277/00; C07C 279/00; C07C 249/00; C07C 69/00; C07C 229/00; C07C 261/00; C07C 327/00; C07C 273/00; C07C 241/00; C07C 243/00; C07D 295/00; C07D 265/30; C07D 239/02; C07D 401/00; C07D 403/00; C07D 405/00; C07D 409/00; C07D 411/00; C07D 419/00; C07D 241/04; C07D 211/26; C07D 211/70; C07D 211/82; C07D 213/55; C07D 211/92; C07D 213/18; C07D 213/20; C07D 263/10; C07D 333/10; C07H 5/04; C07H 5/06; A61K 38/16

ABSTRACT:

Aminimide- and oxazolone-based molecules, and arrays thereof, having at

least two structural diversity elements are made via systematic modular production. A **combinatorial** **library** of aminimide- and oxazolone-based molecules is made via systematic modular production.

WO 09531459A1 Nov. 23, 1995 L8: 14 of 27
MORPHOLINO-SUBUNIT **COMBINATORIAL** **LIBRARY** AND METHOD

INVENTOR: JAMES E SUMMERTON, et al. (1)
ASSIGNEE: ANTIVIRALS INC
APPL NO: US 09506041W
DATE FILED: May 11, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07D 473/00; C07D 417/14; C07H 21/00; C07F 9/6533; C07F 9/6558; C07F 9/6561

ABSTRACT:

A method of generating a compound capable of interacting specifically with a selected macromolecular ligand is disclosed. The method involves contacting the ligand with a **combinatorial** **library** of oligomers composed of morpholino subunits with a variety of nucleobase and non-nucleobase side chains. Oligomer molecules that bind specifically to the receptor are isolated and their sequence of base moieties is determined. Also disclosed is a **combinatorial** **library** of oligomers useful in the method and novel morpholino-subunit polymer compositions.

WO 09530642A1 Nov. 16, 1995 L8: 15 of 27
COMBINATORIAL DIHYDROBENZOPYRAN **LIBRARY**

INVENTOR: JOHN J BALDWIN, et al. (5)
ASSIGNEE: PHARMACOPEIA INC, et al. (6)
APPL NO: US 09505940W
DATE FILED: May 8, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07C 205/06; C07D 311/04; C07D 279/10; C07D 275/02; C07D 207/00; A61K 31/555; A61K 31/54; A61K 31/50; A61K 31/385; A61K 31/35

ABSTRACT:

<CHG DATE=19960103 STATUS=O>**Combinatorial** **libraries** are disclosed which are represented by the Formula (I): (T'-L)q- <S> -C(O)-L'-II' wherein <S> is a solid support; T'-L- is an identifier residue; and -L'-II' is a ligand/linker residue. These **libraries** contain dihydrobenzopyrans of formula (II) which interact (i.e., as agonists or antagonists) with alpha adrenergic receptors, dopamine receptor, sigma -opiate receptors, and K<+> channels and are inhibitors of carbonic anhydrase isozymes. They are useful in the treatment of ocular diseases such as glaucoma.

WO 09528640A1 Oct. 26, 1995 L8: 16 of 27
COMPLEX **COMBINATORIAL** CHEMICAL **LIBRARIES** ENCODED WITH TAGS

INVENTOR: W CLARK STILL, et al. (4)
ASSIGNEE: UNIV COLUMBIA, et al. (6)
APPL NO: US 09504683W
DATE FILED: Apr. 13, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: G01N 33/53

ABSTRACT:

Encoded **combinatorial** chemistry is provided, where sequential synthetic schemes are recorded using organic molecules, which define choice of reactant, and stage, as the same or different bit of information. Various products can be produced in the multi-stage synthesis, such as oligomers and synthetic non-repetitive organic molecules. Conveniently, nested families of compounds can be employed as identifiers, where number and/or position of a substituent define the choice. Alternatively, detectable functionalities may be employed, such as radioisotopes, fluorescers, halogens, and the like, where presence and ratios of two different groups can be used to define stage or choice. Particularly, pluralities of identifiers may be used to provide a binary or higher code, so as to define a plurality of choices with only a few detachable tags. The particles may be screened for a characteristic of interest, particularly binding affinity, where the products may be detached from the particle or retained on the particle. The reaction history of the particles which are positive for the characteristic can be determined by the release of the tags and analysis to define the reaction history of the particle.

WO 09525737A1 Sep. 28, 1995 L8: 17 of 27

METHOD FOR IDENTIFYING MEMBERS OF **COMBINATORIAL** **LIBRARIES**

INVENTOR: STEPHEN J BENKOVIC, et al. (3)
ASSIGNEE: PENN STATE RES FOUND, et al. (4)
APPL NO: US 09503355W
DATE FILED: Mar. 23, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07H 21/00; C07K 1/04

ABSTRACT:

A method to determine the molecular weights of femtomole or smaller quantities of small peptides, oligonucleotides, or heterocyclics covalently attached to addressable polystyrene beads on a grid is presented using imaging time-of-flight secondary ion mass spectrometry (TOF-SIMS). The determination is made possible by selectively clipping the bond linking the peptide, oligonucleotide, or heterocyclic to the bead, followed directly by a TOF-SIMS assay of the bead on the grid. The method can be applied to large numbers of 10-120 micron polystyrene beads having different small molecules attached thereto for direct characterization of massive **combinatorial** **libraries**.

WO 09524186A1 Sep. 14, 1995 L8: 18 of 27
SULFONAMIDE DERIVATIVES AND THEIR USE

INVENTOR: JOHN J BALDWIN, et al. (2)
ASSIGNEE: PHARMACOPEIA INC, et al. (3)
APPL NO: US 09503223W
DATE FILED: Mar. 10, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: A61K 31/095; A61K 38/09; A61K 39/44; C07C 69/06; C07C 211/00; C07C 211/06; C07C 233/19; C07C 233/22; C07C 317/14; C07C 323/22; C07C 323/33; C07D 207/00; C07D 233/54; C07D 285/10; C07D 307/64; C07D 315/00; C07D 333/34; C07D 333/36; C08F 112/08

ABSTRACT:

Combinatorial **libraries** are disclosed which are represented by the formula (I): (T'-L)q- <S> -C(O)-L'-II' wherein: <S> is

a solid support; T'-L- is an identifier residue; and -L'-II' is a ligand/linker residue. These **libraries** contain aryl sulfonamides, N-acyl derivatives, and N-substituted pyrrolidines and piperidines of the formula: Y-A-CO-R<1> which are inhibitors of serine proteases and carbonic anhydrase isozymes. They are useful in the treatment of hyper-coagulation disease and ocular diseases such as glaucoma.

WO 09523163A1 Aug. 31, 1995 L8: 19 of 27
PNA **COMBINATORIAL** **LIBRARIES** AND IMPROVED METHODS OF SYNTHESIS

INVENTOR: PHILIP DAN COOK, et al. (2)
ASSIGNEE: ISIS PHARMACEUTICALS INC, et al. (3)
APPL NO: US 09502182W
DATE FILED: Feb. 22, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07K 1/02; C07K 1/04; C07K 1/06; C07K 1/10; C07K 2/00; C07K 19/00

ABSTRACT:

New sub-monomer synthetic methods for the preparation of peptide nucleic acid oligomeric structures are disclosed that provide for the synthesis of both predefined sequence peptide nucleic acid oligomers as well as random sequence peptide nucleic acid oligomers. Further these methods also provide for the incorporation of peptide nucleic acid units or strings of such units with amino acids or strings of amino acids in chimeric peptide nucleic acid-amino acid compounds. Further disclosed are methods of making random **libraries** of peptide nucleic acids using the fully preformed monomers.

WO 09519359A1 Jul. 20, 1995 L8: 20 of 27
PROCESS FOR MAKING XANTHENE OR CUBANE BASED COMPOUNDS, AND PROTEASE INHIBITORS

INVENTOR: JULIUS JR REBEK, et al. (2)
ASSIGNEE: MASSACHUSETTS INST TECHNOLOGY
APPL NO: US 09500344W
DATE FILED: Jan. 11, 1995
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07D 405/14; A61K 31/35; C07C 61/125; A61K 31/185; C07D 311/82;

A61K 31/40

ABSTRACT:

Methods for forming **combinatorial** **libraries** and the **libraries** produced thereby are provided. According to a preferred aspect of the invention, a plurality of core molecules, the core molecule being a xanthene or cubane derivative, are reacted with a plurality of different tool molecules to form a **library** of molecules having non-naturally occurring molecular diversity. The **libraries** are useful for identifying lead compounds which modulate the functional activity of a biological molecule. Protease inhibitors that have been isolated from the **libraries** also are disclosed.

WO 09516918A1 Jun. 22, 1995 L8: 21 of 27
COMBINATORIAL **LIBRARIES** AND METHODS FOR THEIR USE

INVENTOR: SYDNEY BRENNER
ASSIGNEE: COMBICHEM INC
APPL NO: US 09408542W
DATE FILED: Jul. 26, 1994
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: G01N 33/68; C07K 1/04

ABSTRACT:

Kit, and method for its use and construction, which includes a first plurality of vessels containing different polysubunits, each constructed from a known number of subunits. Each subunit is joined by one or more bonds and each subunit and bond can be the same or different. Each of the different polysubunits has a different sequence of subunits but has the same known subunit at one terminus. Each vessel contains polysubunits which have a different known subunit at one terminus. The kit further includes a second plurality of vessels which includes different polysubunits, each constructed from the known number minus one subunit, as described above.

WO 09516209A1 Jun. 15, 1995 L8: 22 of 27
PROCESS FOR THE PRODUCTION OF **COMBINATORIAL** COMPOUND **LIBRARIES**

INVENTOR: EDUARD FELDER, et al. (2)
ASSIGNEE: CIBA GEIGY AG, et al. (3)

APPL NO: EP 09403936W
DATE FILED: Nov. 28, 1994
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: G01N 33/68; C07K 1/04; C07K 17/00; G01N 33/86; //G01N 33/543; C12Q 1/68; G01N 33/566; G01N 33/58

ABSTRACT:

<CHG DATE=19950726 STATUS=O>The present invention relates to a process for the preparation of a plurality of different units consisting of a solid or semisolid carrier (bead), a synthetic oligomer (ligand) and an identification structure (tag) by means of which the monomers of the ligands are coded, and the use of said **library** for searching for novel classes of compounds and individual compounds. The invention further relates to compounds found with the novel process and the use thereof as thrombin inhibitors.

WO 09426787A1 Nov. 24, 1994 L8: 23 of 27
METHOD FOR GENERATING CELL TYPE SPECIFIC PHAGE ANTIBODY **LIBRARIES**

INVENTOR: WILLIAM T TSE, et al. (1)
ASSIGNEE: UNIV LELAND STANFORD JUNIOR
APPL NO: US 09405124W
DATE FILED: May 4, 1994
PATENT ABSTRACTS OF EUROPE
ABS GRP NO:
ABS VOL NO:
ABS PUB DATE:
INT-CL: C07K 15/28

ABSTRACT:

A method for generating monoclonal antibodies directed against previously uncharacterized an unpurified antigens on the surface of target cells in a cell population. The method includes incubating (100) a **combinatorial** **library** of antibodies expressed on the surface of filamentous phage particles with a target cell population under conditions sufficient to bind a portion of the phage particles to the target cells. The target cells and bound phage particles are then separated (102) from the unbound phage particles, and the bound phage particles are recovered (104). These phage particles are then amplified (106) to create an enriched **library**. Monoclonal antibodies specific

to the target cell are then isolated (108) from the enriched **library** for subsequent use.

WO 09408051A1 Apr. 14, 1994 L8: 24 of 27
COMPLEX **COMBINATORIAL** CHEMICAL **LIBRARIES** ENCODED WITH TAGS

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INT-CL: C12Q 1/68; C07H 21/02; C07H 21/04; A61K 48/00; A61K 37/00

ABSTRACT:

Encoded **combinatorial** chemistry is provided, where sequential synthetic schemes are recorded using organic molecules, which define choice of reactant, and stage, as the same or different bit of information. Various products can be produced in the multi-stage synthesis, such as oligomers and synthetic non-repetitive organic molecules. Conveniently, nested families of compounds can be employed as identifiers, where number and/or position of a substituent define the choice. Alternatively, detectable functionalities may be employed, such as radioisotopes, fluorescers, halogens, and the like, where presence and ratios of two different groups can be used to define stage or choice. Particularly, pluralities of identifiers may be used to provide a binary or higher code, so as to define a plurality of choices with only a few detachable tags. The particles may be screened for a characteristic of interest, particularly binding affinity, where the products may be detached from the particle or retained on the particle. The reaction history of the particles which are positive for the characteristic can be determined by the release of the tags and analysis to define the reaction history of the particle.

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SPECIFICATION METHOD AND APPARATUS FOR PEPTIDE SYNTHESIS AND SCREENING

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INT-CL: B01D 25/12; B01D 63/00; B01J 19/00; B01L 9/00; B01L 11/00; C08F 283/00; C08F 285/00; C07H 21/00; C07K 1/06; C07K 5/00; C07K 7/00; C07K 15/00; C07K 17/00; C08L 89/00; C12Q 1/00; C12P 19/04; C12P 19/38; C12P 21/06; G01N 21/00; G01N 33/00; G01N 33/543; G01N 33/544; G01N 33/545; G01N 33/546; G01N 33/552

ABSTRACT:

Method and apparatus for synthesizing a **combinatorial** **library** of families of biopolymers, such as polypeptides, oligonucleotides and oligosaccharides, on a reusable, spatially addressable solid phase plate (5'), typically in arrays of 4x4 to 400x400. In the case of peptides, such as synthesis of hexapeptides, the **library** contains one to three, typically two, positions in the sequence which are uniquely identified by the spatial address location. The preferred plate (5') embodiment employs a hydrophilic polar multi-functionalized polymer film coating discs or "winks" (50) of porous polyolefin which are removably received in holes (51) in the plate (5'). The plate (5') is employed with a vacuum block system (46, 47, 48) to assist in washing, deprotection of protected monomers, such as FMOC protected amino acids, and screening of immobilized, synthesized hexapeptides, for example, to determine which synthetic hexapeptides specifically bind to functional target proteins, such as enzymes, receptors and antibodies. Following identification of the known synthetic polypeptides giving the greatest affinity for the arrayed positions in the sequence, optimal binding for the complete peptide sequence is determined by an iterative process replacing formerly mixed positions with known amino acids at defined spatial addresses.

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ENCODED **COMBINATORIAL** CHEMICAL **LIBRARIES**

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APPL NO: US 09303127W
DATE FILED: Mar. 30, 1993
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INT-CL: C12Q 1/70; C07K 5/00; C07K 13/00; G01N 33/53

ABSTRACT:

The present invention describes an encoded **combinatorial** chemical **library** comprised of a plurality of bifunctional molecules having both a chemical polymer and an identifier oligonucleotide sequence that defines the structure of the chemical polymer. Also described are the bifunctional molecules of the **library**, and methods of using the **library** to identify chemical structures within the **library** that bind to biologically active molecules in preselected binding interactions.

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PRODUCTION OF CHIMERIC ANTIBODIES - A **COMBINATORIAL** APPROACH

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DATE FILED: Sep. 23, 1992
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INT-CL: C07K 13/00; C12N 15/00; C12N 15/13; C12N 15/62

ABSTRACT:

Methods are disclosed which may be used for the production of antibodies, or antibody fragments, which have the same binding specificity as a parent antibody but which have increased human characteristics. Humanised antibodies may be obtained by chain shuffling, perhaps using phage display technology. In one embodiment, a polypeptide comprising a heavy or light chain variable domain of a non-human antibody specific for an antigen of interest is combined with a repertoire of human complementary (light or heavy) chain variable domains. Hybrid pairings which are specific for the antigen of interest are selected. Human chains from the selected pairings may then be combined with a repertoire of human complementary variable domains (heavy or light) and humanised antibody polypeptide dimers can then be selected for binding specificity for antigen. The methods may be combined with CDR-imprinting. In another embodiment, component part of an antigen-binding site of a non-human antibody known to bind a particular antigen is combined with a repertoire of component parts of an antigen-binding site of human antibody, forming a **library** of antibody polypeptide dimers with antigen-binding sites. Hybrids selected from this **library** may be used in a second humanising shuffling step, or may already be of sufficient human character to be of value, perhaps after some modification to increase human character still further.
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